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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

LI, QIAN J

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 04 09 2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/485,421

Applicant(s)

MAHALINGAM ET AL.

Examiner

Janice Li

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 25 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: detailed action

DETAILED ACTION

The amendment filed on January 25, 2002 has been entered as Paper #13.
Claims 12-27 have been cancelled, claims 1 and 11 have been amended.
Claims 1-11 are pending in the application and under current examination.
The previous objection and rejections that do not reiterated in this Office action are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION REQUIREMENT

The prior rejection of claims 1-11 stands for the reasons advanced on pages 5-7 of the prior Office action (paper No. 11), and applies to the newly amended claims.

The applicants argue in Paper # 13 that the specification provides definition for "non-Vpr protein" in page 7, that one skilled in the art would readily understand that this refers to a protein that is not identical to HIV Vpr protein but comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein, which is the distinguishing identifying characteristic of the protein.

The arguments have been carefully considered but found not persuasive. This is because the claims and the specification essentially do not place any limit on the length

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of the "non-HIV-1 Vpr protein", the number of amino acids that could be additionally included, thus the scope of the claims includes numerous structural variants, or even non-related proteins, which may comprising the recited 19 or 25 amino acid sequences but functionally irrelevant to the delivery of nucleic acids. An adequate written description of a protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself. It is not sufficient to define the protein solely by one short fragment it contains, because it is the three-dimensional structure of the polypeptide that allows a protein to function, and such function requires proper dimerization, and in the instant case, proper interaction with the cellular and nuclear membrane, and thus nucleus transport. Neither art of record nor the specification teaches that any length of a protein comprising the recited fragments would function to promote nucleus transport of a nucleic acid or any therapeutic compound. The function of an amino acid fragment in the context of a polypeptide sequence is not as simple as placing a CD player in an automobile. Even minor changes in the type of amino acids neighboring the fragment, or in the total length of the polypeptide the fragment seated in, may change the functional characteristics of the fragment. Determination of the function of a particular "non-HIV-1 Vpr protein" is not predictable until they are actually made and used, hence resulting in a trial and error situation. Therefore, the general knowledge and levels of skill in the art do not supplement the omitted description, because specific, not general guidance is what is needed. One cannot extrapolate the teachings of the specification to the scope of the claims because the skilled artisan

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cannot envision the detailed structure of polypeptides encompassed by these claims and whether these polypeptides can serve as a functional transporter. The skilled artisan cannot envision the detailed chemical structure of all encompassed proteins. Therefore, the disclosure does not allow one skilled in the relevant art to recognize that applicants had possession of claimed invention commensurate to its scope.

For the reasons of record and those set forth above, the instant specification fails to meet the written description requirement for the broad scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5-11 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO9608970.

Applicants argue that the fragments recited in the claims could not be located in the cited publication, and the fragments recited in page 53 of WO9608970 do not include the residues 17-36 and/or 59-84 of Vpr protein.

The argument has been carefully considered but found not persuasive because claim 1 uses open language "comprising". WO9608970 teaches, in page 53, lines 13-30, a Vpr protein or its fragment, that the fragments could be any Vpr residues in a length of 3-25 amino acids, which could comprising the instantly recited fragments.

Therefore, the fragments recited in claim 1 are embraced by the cited teaching, thus, WO9608970 anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO9608970 as applied to claims 1, 3, 5-11 above, and further in view of *Katz et al* (US 6,005,004) or *Kayyem et al* (US 6,232,295).

Applicants argue that the WO9608970 reference does not teach or suggest fragments of vpr as recited in claim 1, neither *Katz* reference nor the *Kayyem* reference teach such fragments. Thus, the combination of teachings fails to produce the instantly claimed invention.

The argument has been carefully considered but found not persuasive because claim 1 uses open language "comprising". WO9608970 teaches in page 53, lines 18-30 that the fragments could be any Vpr protein or fragments in a length of 3-25 amino acids. Therefore, the fragments recited in claim 1 are embraced by the WO9608970 teaching.

The *Katz* reference teaches to selectively transport therapeutic material to brain cells using lipophilic-polycationic delivery systems comprising a biologically active

molecule covalently bonded with cationic carriers and permeabilizer peptides to overcome the difficulty and enhance efficiency for drug delivery to neuronal cells (see abstract). They go on to teach such biologically active molecules comprise polypeptides, nucleic acids, oligonucleotides and transfection vectors (see claims 1-5). The *Kayyem* reference teaches a gene delivery system comprises polymeric molecule complexed with a nucleic acid vector and attached to at least one cell targeting moiety and using such for intracellular delivery (claims 1& 2), Kayyem et al teach that such polymeric molecule will improve the current liposome system for cell specific genetic material delivery (Column 2, paragraphs 4-6).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of *WO9608970*, by simply including a polycationic peptide sequence to the vpr conjugated composition to further enhance intracellular delivery of nucleic acids as taught by *Katz et al* or *Kayyem et al*. The ordinary skilled artisan would have been motivated to do so for efficient intracellular drug delivery with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
April 2, 2002

JAMES KETTER
PRIMARY EXAMINER